Supporting Information

Tuning the Coordination Properties of Chiral Pseudopeptide Bis(2-picolyl)amine and Iminodiacetamide Ligands in Zn(II) and Cu(II) Complexes

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1 List of abbreviations

Ala – Alanine

γ-Abu-OH – γ-Aminobutyric acid

HOBt – Hydroxybenzotriazole

TBTU – 2-(1H-Benzotriazole-1-yl)-1,1,3,3-tetramethylaminium tetrafluoroborate

DIPEA – N,N-Diisopropylethylamine

Phe – Phenylalanine

Boc – tert-Butyloxycarbonyl

VT NMR – variable temperature NMR
2 Synthesis

2.1 General procedure for the synthesis of Boc-protected precursors.

![Figure S1. Synthesis of Boc-protected precursors Boc2A-Boc3C](image)

A solution of the acid (1 equiv.), HOBT (1 equiv.), TBTU (1 equiv.) and DIPEA (4 equiv.) in dichloromethane (100 mL) was stirred at room temperature for 1 h. Then, the amine (1.0 or 1.5 equiv.) was added and stirring continued for 2 days. The reaction mixture was washed with aqueous sodium bicarbonate and brine, the organic layer dried over anhydrous sodium sulphate, filtered, and evaporated in a vacuum. The crude product was purified by automated flash chromatography (Teledyne Isco CombiFlash Rf) on pre-packed silica columns.

**Boc2A.** Boc-\(\beta\)-Ala-OH (700 mg, 3.7 mmol), (S)-(−)-1-phenylethylamine (706 μL, 5.6 mmol), HOBT (500 mg, 3.7 mmol), TBTU (1188 mg, 3.7 mmol), DIPEA (2.5 mL, 14.8 mmol). Automated flash chromatography (silica gel) 50% → 100% ethyl acetate in 60% ethyl acetate in hexane. Yield: 76% (841 mg, 2.4 mmol), white powder. \(^1^H\) NMR (300.13 MHz, CDCl\(_3\)) \(\delta\) 7.32 – 7.26 (m, 3H, Ph), 5.94 (s, 1H, NH), 5.16 – 5.07 (m, 2H, CH), 4.87 (m, 1H, CH\(_3\)), 3.44 – 3.36 (m, 2H, CH\(_2\)), 2.48 – 2.34 (m, 2H, CH\(_3\)), 1.48 (d, \(J = 6.9\) Hz, 3H, CH\(_3\)), 1.42 (s, 9H, Boc).

**Boc2B.** Boc-\(\beta\)-Ala-OH (600 mg, 3.2 mmol), L-Phe-OMe-HCl (1026 mg, 4.8 mmol), HOBT (428 mg, 3.2 mmol), TBTU (1018 mg, 3.2 mmol), DIPEA (2.1 mL, 12.7 mmol). Automated flash chromatography (silica gel) 20% → 60% ethyl acetate in 60% ethyl acetate in hexane. Yield: 76% (841 mg, 2.4 mmol), white powder. \(^1^H\) NMR (300.13 MHz, CDCl\(_3\)) \(\delta\) 7.32 – 7.26 (m, 3H, Ph), 7.14 – 7.04 (m, 2H, Ph), 5.97 (s, 1H, NH), 5.07 (s, 1H, NH), 4.87 (m, 1H, CH\(_3\)), 3.74 (s, 3H, CH\(_3\)), 3.44 – 3.30 (m, 2H, CH\(_2\)), 3.20 – 3.03 (m, 2H, CH\(_2\)(Ph)), 2.43 – 2.31 (m, 2H, CH\(_3\)), 1.43 (s, 9H, Boc).

**Boc3A.** Boc-\(\gamma\)-Abu-OH (500 mg, 2.5 mmol), (S)-(−)-1-phenylethylamine (470 μL, 3.7 mmol), HOBT (332 mg, 2.5 mmol), TBTU (790 mg, 2.5 mmol), DIPEA (1.6 mL, 9.8 mmol). Automated flash chromatography (silica gel) 30% → 70% ethyl acetate in 60% ethyl acetate in hexane. Yield: 94% (705 mg, 2.3 mmol), white solid. \(^1^H\) NMR (600.13 MHz, CDCl\(_3\)) \(\delta\) 7.39 – 7.30 (m, 3H, Ph), 6.40 (s, 1H, NH), 5.16 – 5.08 (m, 1H, CH), 4.72 (s, 1H, NH), 4.23 – 3.10 (m, 2H, CH\(_2\)), 2.21 (t, \(J = 7.0\) Hz, 2H, CH\(_2\)), 1.88 – 1.73 (m, 2H, CH\(_2\)), 1.49 (d, \(J = 6.9\) Hz, 3H, CH\(_3\)), 1.44 (s, 9H, Boc).

**Boc3B.** Boc-\(\gamma\)-Abu-OH (500 mg, 2.5 mmol), L-Phe-OMe-HCl (796 mg, 3.7 mmol), HOBT (332 mg, 2.5 mmol), TBTU (790 mg, 2.5 mmol), DIPEA (1.6 mL, 9.8 mmol). Automated flash chromatography (silica gel) 30% → 70% ethyl acetate in hexane. Yield: 96% (858 mg, 2.4 mmol), white solid. \(^1^H\) NMR (600.13 MHz, CDCl\(_3\)) \(\delta\) 7.33 – 7.27 (m, 2H, Ph), 7.26 – 7.22 (m, 1H, Ph), 7.21 – 7.17 (m, 1H, Ph), 7.13 (d, \(J = 7.0\) Hz, 1H, Ph), 6.41 (s, 1H, NH), 4.90 – 4.82 (m, 1H, CH), 4.69 (s, 1H, NH), 3.73 (m, 3H, CH\(_3\)), 3.24 – 3.13 (m, 2H, CH\(_2\)), 3.13 – 3.03 (m, 2H, CH\(_2\)), 2.25 – 2.14 (m, 2H, CH\(_2\)), 1.81 – 1.71 (m, 2H, CH\(_2\)), 1.44 (s, 9H, Boc).

**Boc3C.** N-Acetyl-L-phenylalanine (595 mg, 2.9 mmol), N-Boc-1,3-propanediamine (501 μL, 2.9 mmol), HOBT (388 mg, 2.9 mmol), TBTU (922 mg, 2.9 mmol), DIPEA (1.9 mL, 11.5 mmol). Automated flash chromatography (silica gel) 20% → 100% ethyl acetate in hexane. Yield: 95% (865 mg, 2.9 mmol), white solid. \(^1^H\) NMR (600.13 MHz, CDCl\(_3\)) \(\delta\) 7.33 – 7.27 (m, 2H, Ph), 7.26 – 7.22 (m, 1H, Ph), 7.21 – 7.17 (m, 1H, Ph), 7.13 (d, \(J = 7.0\) Hz, 1H, Ph), 6.41 (s, 1H, NH), 4.90 – 4.82 (m, 1H, CH), 4.69 (s, 1H, NH), 3.73 (m, 3H, CH\(_3\)), 3.24 – 3.13 (m, 2H, CH\(_2\)), 3.13 – 3.03 (m, 2H, CH\(_2\)), 2.25 – 2.14 (m, 2H, CH\(_2\)), 1.81 – 1.71 (m, 2H, CH\(_2\)), 1.44 (s, 9H, Boc).
chromatography (silica gel) 0% → 5% methanol in dichloromethane, \( R_f = 0.24 \), 5% methanol in dichloromethane. Yield: 87% (903 mg, 2.5 mmol), white solid. \(^1\)H NMR (300.13 MHz, CDCl\(_3\)) \( \delta \) 7.35 – 7.27 (m, 2H, Ph), 7.24 – 7.17 (m, 3H, Ph), 6.49 (s, 1H, NH), 6.13 (d, \( J = 7.2 \) Hz, 1H, NH), 4.73 (s, 1H, NH), 4.69 – 4.56 (m, 1H, CH), 3.23 – 3.09 (m, 3H, CH\(_2\)), 3.04 – 2.89 (m, 3H, CH\(_2\)), 2.00 (s, 3H, CH\(_3\)), 1.49 – 1.44 (m, 2H, CH\(_2\)), 1.42 (s, 9H, Boc).

2.2 Ligand synthesis

![Figure S2. Synthesis of ligand b1A](image)

![Figure S3. Synthesis of ligand b2C](image)

![Figure S4. Synthesis of ligands b2A-i3C](image)
3 Structures of the synthesized ligands and truncated ligands used in calculations

Figure S5. Structures of twelve synthesized ligands and nine truncated ligand models used in calculations.

Figure S6. Nomenclature for the ligand structure used throughout the text.
4 NMR spectroscopy of free ligands

4.1 $^1$H NMR spectra of free ligands in different solvents

The extent of hydrogen bonding can be inferred from the comparison of amide proton $^1$H NMR chemical shifts in DMSO and chloroform using the hydrogen bond acidity value, $A$ (Table S1).$^1$ Large $A$ values indicate that the side chain amide protons of i2A and i3A are not significantly hydrogen-bonded in chloroform. A weak hydrogen bond is likely in b3A, as the amide proton is shifted 0.5 ppm more downfield than in i3A with an isostructural side chain. Hydrogen bonding of the side chain amide is less likely in the imda derivatives, as the chelator amides compete for hydrogen bonding by forming 5-membered rings. In b1A and b2A the amide peak is shifted downfield in chloroform compared to DMSO due to strong hydrogen bonding in chloroform.

Table S1. $^1$H NMR peaks of the side chain amide protons in different solvents at 6 - 8 mM concentrations.

<table>
<thead>
<tr>
<th>Ligand</th>
<th>$\delta$(DMSO) /ppm</th>
<th>$\delta$(CDCl$_3$) /ppm</th>
<th>$\Delta\delta$</th>
<th>$A^b$</th>
<th>$\delta$(CD$_3$CN) /ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>b1A</td>
<td>8.95</td>
<td>9.24</td>
<td>-0.29</td>
<td>-0.03</td>
<td>9.12</td>
</tr>
<tr>
<td>b2A</td>
<td>8.39</td>
<td>8.51</td>
<td>-0.12</td>
<td>-0.01</td>
<td>7.93</td>
</tr>
<tr>
<td>b3A</td>
<td>8.18</td>
<td>6.43</td>
<td>1.75</td>
<td>0.24</td>
<td>6.83</td>
</tr>
<tr>
<td>i2A</td>
<td>8.49</td>
<td>5.92</td>
<td>2.57</td>
<td>0.35</td>
<td>7.17$^d$</td>
</tr>
<tr>
<td>i3A</td>
<td>8.22</td>
<td>5.96</td>
<td>2.26</td>
<td>0.31</td>
<td>6.93</td>
</tr>
<tr>
<td>lit.$^c$</td>
<td>7.73</td>
<td>5.42</td>
<td>2.31</td>
<td>0.31</td>
<td>6.23</td>
</tr>
</tbody>
</table>

$^a$$\Delta\delta = \delta$(DMSO) – $\delta$(CDCl$_3$), $^bA = 0.0065 + 0.133\Delta\delta$, $^c$the side chain NH peak of i2A in CD$_3$CN is overlapped with the phenyl peaks, $^dlit. = N$-methylacetamide as an example of a non-hydrogen bonded amide from ref.$^{1,2}$

Figure S7. $^1$H NMR spectra (aromatic region) of ligand b1A in DMSO-$d_6$ (7.9 mM), chloroform-$d_3$ (7.9 mM), and acetonitrile-$d_3$ (7.7 mM). Side chain amide NH protons (*) are accented.
Figure S8. $^1$H NMR spectra (aromatic region) of ligand b2A (left) in DMSO-$d_6$ (5.8 mM), chloroform-$d_3$ (6.1 mM), and acetonitrile-$d_3$ (6.1 mM), and ligand b3A (right) in DMSO-$d_6$ (7.0 mM), chloroform-$d_3$ (6.8 mM), and acetonitrile-$d_3$ (7.0 mM). Side chain amide NH protons (*) are accented.

Figure S9. $^1$H NMR spectra (aromatic region) of ligand i2A (left) in DMSO-$d_6$ (6.0 mM), chloroform-$d_3$ (6.0 mM), and acetonitrile-$d_3$ (6.2 mM). The NH peak in acetonitrile solution is overlapping with the aromatic signals. $^1$H NMR spectra (aromatic region) of ligand i3A (right) in DMSO-$d_6$ (8.0 mM), chloroform-$d_3$ (7.7 mM), and acetonitrile-$d_3$ (8.0 mM). Side chain amide NH protons (*) are accented.

4.2 Variable concentration $^1$H NMR spectra of free ligands

Figure S10. Variable concentration $^1$H NMR spectra (aromatic region) of ligand b1A in acetonitrile-$d_3$. Side chain amide NH protons (*) are accented.
Figure S11. Variable concentration $^1$H NMR spectra (aromatic region) of ligand b2A (left) and ligand b3A (right) in acetonitrile-$d_3$. Side chain amide NH protons (*) are accented.

Figure S12. Variable concentration $^1$H NMR spectra (aromatic region) of ligand b2B (left) and ligand b3B (right) in acetonitrile-$d_3$. Side chain amide NH protons (*) are accented.

Figure S13. Variable concentration $^1$H NMR spectra (aromatic region) of ligand b2C (left) and ligand b3C (right) in acetonitrile-$d_3$. Side chain amide NH protons (*) are accented.
Figure S14. Variable concentration $^1$H NMR spectra (aromatic region, the NH peak is overlapping with the aromatic signals) of ligand i2A (left) and ligand i3A (right) in acetonitrile-$d_3$. Side chain amide NH protons (*) are accented.

Figure S15. Variable concentration $^1$H NMR spectra (aromatic region, the NH peak is overlapping with the aromatic signals) of ligand i2B (left) and ligand i3B (right) in acetonitrile-$d_3$. Side chain amide NH protons (*) are accented.

Figure S16. Concentration dependence of side chain NH peak shifts in acetonitrile-$d_3$. $^1$H NMR of Ligand i3C was measured only at a lower concentration due to poor solubility.
4.3 COSY NMR spectrum of b3A

Figure S17. COSY spectrum of ligand b3A (7.4 mM, aromatic region) in acetonitrile-d$_3$.

Figure S18. COSY spectrum of ligand b3A (7.4 mM, aliphatic region) in acetonitrile-d$_3$. 

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4.4  $^1\text{H}-^1\text{H}$ NOESY spectra of free ligands

Figure S19. NOESY interactions of side chain amide NH peaks in ligands $b_{1A}$, $b_{2A}$, and $b_{3A}$.

5  IR spectroscopy of free ligands

IR spectra in dichloromethane (Figure S16) show a significantly higher ratio of bonded amides with N-H vibrations below 3400 cm$^{-1}$ for $b_{2A}$ than $b_{3A}$, in agreement with the strong and weak hydrogen bonds observed in NMR for $b_{2A}$ and $b_{3A}$, respectively.$^3$ The situation is different for $i_{2A}$ and $i_{3A}$, where the aliphatic linker length had no effect on the ratio of free and bonded amides, indicating that the side chain amides in $i_{2A}$ and $i_{3A}$ are not significantly hydrogen bonded due to competition with the chelator amides. Variable concentration IR spectra (Figures S17-S18) show no change for $b_{2A}$, suggesting intramolecular hydrogen bonding, while $b_{3A}$, $i_{2A}$ and $i_{3A}$ with amide groups available for aggregation show an increase of the bonded N-H peak at higher concentrations.

Figure S20. IR spectra in dichloromethane solution at $c \approx 10$ mM
Figure S21. Variable concentration IR spectra of \textbf{b2A} (left) and of \textbf{b3A} (right) corrected for concentration in dichloromethane.

Figure S22. Variable concentration IR spectra of \textbf{i2A} (left) and of \textbf{i3A} (right) corrected for concentration in dichloromethane.
Figure S23. Molecular structures of b2A-Cu-o (a) and b2A-Cu-t (b) with thermal ellipsoids drawn at the 30% probability level. (c) Molecular overlap representation showing differences in conformation of [Cu(b2A)(H2O)(CF3SO3)]+ cations in orthorhombic (dark colours) and triclinic forms (light colours).
Figure S24. Molecular structure of i3A-Cu with thermal ellipsoids drawn at the 30% probability level. Atoms from the disordered triflate anion with site occupancies lower than 0.5 are shown with empty ellipsoids (disorder part b).

Figure S25. Molecular structure of i3B-Cu with thermal ellipsoids drawn at the 30% probability level. Atoms from the disordered perchlorate anion and a nitromethane solvent molecule with site occupancies lower than 0.5 are shown with dashed empty ellipsoids (disorder parts b), other atoms from nitromethane solvent molecules are shown as empty ellipsoids.
Figure S26. Molecular structure of i3B-Ni with thermal ellipsoids drawn at the 30% probability level. Atoms from the nitromethane solvent molecule with site occupancies lower than 0.5 are shown with dashed empty ellipsoids, other atoms from nitromethane solvent molecules are shown as empty ellipsoids.

Figure S27. X-ray powder diffractogram of b2A-Cu. Red curve is the calculated diffractogram based on Rietveld refinement considering both phases obtained from the single crystal X-ray diffraction (b2A-Cu-o and b2A-Cu-t). The majority of observed peaks agreed with b2A-Cu-o or b2A-Cu-t phases, additional peaks (thin black lines) show contribution of an additional unknown crystalline phase in the sample. Refined values for phase fractions of b2A-Cu-o and b2A-Cu-t phases were 0.47(3) and 0.53(3), respectively ($R_{wp} = 19.41\%$). Refinement was performed with the GSAS-II program.4
Figure S28. Crystal packing diagram of b2A-Cu-o (a) and b2A-Cu-t (b). Complex cations are shown in red, coordinated triflate anions in yellow, and free triflate anions in blue. Contents of the original asymmetric unit of b2A-Cu-o are shown in dark red, yellow, and blue.
Figure S29. Crystal packing diagram of i3A-Cu. Complex cations are shown in red, disordered triflate anions in yellow, regular triflate anions in blue and positions of oxygen atoms from solvent water are coloured green. Contents of the original asymmetric unit are shown in dark red, yellow, blue, and green.

Figure S30. Crystal packing diagram of i3B-Cu. Complex cations are shown in red, perchlorate anions in blue and, nitromethane solvent molecules in green. Contents of the original asymmetric unit are shown in dark red, blue, and green.

Figure S31. Crystal packing diagram of i3B-Ni. Complex cations are shown in red, perchlorate anions in blue, and nitromethane solvent molecules in green.
### Table S2. Experimental data for the X-ray diffraction studies.

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<th>Compound</th>
<th>b2A-Cu-o</th>
<th>b2A-Cu-t</th>
<th>i3A-Cu</th>
<th>i3B-Cu</th>
<th>i3B-Ni</th>
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<td>Formula</td>
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<td>Cu₂H₂CuF₄₇N₀₃S₁</td>
<td>Cu₂H₂CuF₄₇N₀₃S₁</td>
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<td>Flack parameter</td>
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<td>-0.063(6)</td>
<td>0.041(19)</td>
<td>0.00(3)</td>
<td>-0.008(16)</td>
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<tr>
<td>R₁ (I &gt; 2σ(I))</td>
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<td>0.0531</td>
<td>0.0974</td>
<td>0.0773</td>
<td>0.0520</td>
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<tr>
<td>wR₂ (all data)</td>
<td>0.1135</td>
<td>0.1472</td>
<td>0.2806</td>
<td>0.2077</td>
<td>0.1437</td>
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<td>1.031</td>
<td>1.161</td>
<td>1.015</td>
<td>1.044</td>
</tr>
<tr>
<td>Maximum/minimum electron density (e Å⁻³)</td>
<td>0.229/−0.282</td>
<td>0.931/−0.471</td>
<td>0.808/−0.743</td>
<td>1.054/−1.012</td>
<td>0.880/−0.575</td>
</tr>
</tbody>
</table>

[¹] R₁ = Σ ||Fₒ|| − |F_c| / Σ |F_c|, [²] wR₂ = Σ[w(F_c² − F_c)²]/Σ[w(F_c)²]², [³] S = Σ[w(F_c² − F_c)²]/(n − p) where n is number of reflections and p is the total number of parameters refined.

### Table S3. Selected geometrical parameters of ML and ML₂ complexes and geometry determined using FindGeo.⁵

#### ML Complex

<table>
<thead>
<tr>
<th>Nₚv-M-Nₛv / °</th>
<th>Geometry (FindGeo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>b2A-Cu-o</td>
<td>164.26 Octahedron (regular), RMSD = 0.284</td>
</tr>
<tr>
<td>b2B-Cu-t</td>
<td>160.91 Octahedron (regular), RMSD = 0.321</td>
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</tbody>
</table>

#### ML₂ Complex

<table>
<thead>
<tr>
<th>carbonyl-M-carbonyl / °</th>
<th>N₂-M-N₂ / °</th>
<th>Geometry (FindGeo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>i3A-Cu</td>
<td>97.85, 98.25</td>
<td>177.67 Octahedron (regular), RMSD = 0.422</td>
</tr>
<tr>
<td>i3B-Cu</td>
<td>80.86, 105.45</td>
<td>173.26 Octahedron (distorted), RMSD = 0.481</td>
</tr>
<tr>
<td>i3B-Ni</td>
<td>86.10, 96.78</td>
<td>172.12 Octahedron (regular), RMSD = 0.296</td>
</tr>
</tbody>
</table>

### Table S4. Hydrogen bond parameters

<table>
<thead>
<tr>
<th>Hydrogen bond</th>
<th>D−H</th>
<th>H−A</th>
<th>D−A</th>
<th>D−H−A</th>
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</thead>
<tbody>
<tr>
<td>b2A-Cu-o</td>
<td>0.79(4)</td>
<td>2.02(5)</td>
<td>2.726(5)</td>
<td>148(5)</td>
</tr>
<tr>
<td>O1W−H1W−O2T1</td>
<td>0.82(8)</td>
<td>1.92(9)</td>
<td>2.718(5)</td>
<td>166(9)</td>
</tr>
<tr>
<td>N4−H4N−O3T2</td>
<td>0.86(5)</td>
<td>2.05(4)</td>
<td>2.883(6)</td>
<td>166(5)</td>
</tr>
</tbody>
</table>

Symmetry code (i): 1/2+x, 1/2-y, -z

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<table>
<thead>
<tr>
<th>Bond</th>
<th>Distance</th>
<th>Angle</th>
</tr>
</thead>
<tbody>
<tr>
<td>O1W–H1W···O1T2</td>
<td>0.80(2)</td>
<td>1.98(4)</td>
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<tr>
<td>O1W–H2W···O3T1</td>
<td>0.81(6)</td>
<td>1.90(6)</td>
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<tr>
<td>N4–H4N···O2T2'</td>
<td>0.86(7)</td>
<td>2.01(7)</td>
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Symmetry code (i): x, 1+y, z

**i3A-Cu**

<table>
<thead>
<tr>
<th>Bond</th>
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<th>Angle</th>
</tr>
</thead>
<tbody>
<tr>
<td>N11–H11A···O1T2 [B]</td>
<td>0.86</td>
<td>1.93 [2.03]</td>
</tr>
<tr>
<td>N12–H12A···O2T1</td>
<td>0.86</td>
<td>2.01</td>
</tr>
<tr>
<td>N31–H31A···O1W1</td>
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</tr>
<tr>
<td>N31–H32A···O1W2</td>
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<td>2.01</td>
</tr>
<tr>
<td>N41–H41A···O2T1 [B]</td>
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<td>2.19 [2.16]</td>
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<tr>
<td>N42–H42A···O1T1</td>
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Symmetry code (i): x, 1+y, z

**i3B-Cu**

<table>
<thead>
<tr>
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<th>Distance</th>
<th>Angle</th>
</tr>
</thead>
<tbody>
<tr>
<td>N11–H11N···O32</td>
<td>0.80(6)</td>
<td>2.06(8)</td>
</tr>
<tr>
<td>N12–H12N···O2P1 [ii]</td>
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<td>2.17(5)</td>
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<tr>
<td>N31–H31N···O3P1</td>
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<td>2.35(5)</td>
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<td>2.17(6)</td>
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<tr>
<td>N41–H41N···O41 (intra)</td>
<td>0.81(7)</td>
<td>2.36(7)</td>
</tr>
<tr>
<td>N42–H42N···O42 (intra)</td>
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<td>2.34(7)</td>
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</table>

Symmetry codes (i): 1+x, y, z; (ii): -1+x, y, z

**i3B-Ni**

<table>
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<th>Bond</th>
<th>Distance</th>
<th>Angle</th>
</tr>
</thead>
<tbody>
<tr>
<td>N11–H11N···O32 [i]</td>
<td>0.81(6)</td>
<td>1.97(6)</td>
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<tr>
<td>N12–H12N···O2P1 [i]</td>
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<td>2.19(5)</td>
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<tr>
<td>N31–H31N···O3P1</td>
<td>0.81(8)</td>
<td>2.32(8)</td>
</tr>
<tr>
<td>N32–H32N···O1P2</td>
<td>0.82(5)</td>
<td>2.08(5)</td>
</tr>
<tr>
<td>N41–H41N···O42 [iii]</td>
<td>0.81(6)</td>
<td>2.54(6)</td>
</tr>
<tr>
<td>N42–H42N···O42 (intra)</td>
<td>0.80(7)</td>
<td>2.37(7)</td>
</tr>
</tbody>
</table>

Symmetry codes (i): 1+x, y, z; (ii): -1+x, y, z; (iii): 1-x, 1+y, z

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![Diagram of the molecular structure](image)
Figure S32. Hydrogen bonds in \textbf{b2A-Cu-o} (a) and \textbf{b2A-Cu-t} (b). Parameters and symmetry codes are given in Table S4.

Figure S33. Hydrogen bonds in \textbf{i3A-Cu}. Parameters and symmetry codes are given in Table S4.
Figure S34. Intermolecular hydrogen bonds in 13B-Cu. Parameters and symmetry codes are given in Table S4.

Figure S35. Intermolecular hydrogen bonds in 13B-Ni. Parameters and symmetry codes are given in Table S4.
7 Cu(II) complexes

7.1 UV-Vis spectroscopy

Figure S36. UV-Vis spectra for the titration of Cu(II) (3.22 mM) with ligand b1A in acetonitrile.

Figure S37. UV-Vis spectra for the titration of Cu(II) (3.41 mM) with ligand b2A in acetonitrile.
Figure S38. UV-Vis spectra for the titration of Cu(II) (3.41 mM) with ligand b2B in acetonitrile.

Figure S39. UV-Vis spectra for the titration of Cu(II) (3.13 mM) with ligand b2C in acetonitrile.
Figure S40. UV-Vis spectra and titration curve for the titration of Cu(II) (3.33 mM) with ligand b3A in acetonitrile.

Figure S41. UV-Vis spectra for the titration of Cu(II) (3.33 mM) with ligand b3B in acetonitrile.
Figure S42. UV-Vis spectra for the titration of Cu(II) (3.38 mM) with ligand $b_3C$ in acetonitrile.

Figure S43. UV-Vis spectra for the titration of Cu(II) (3.24 mM) with ligand $i_2A$ in acetonitrile.
Figure S44. UV-Vis spectra for the titration of Cu(II) (3.04 mM) with ligand i2B in acetonitrile.

Figure S45. UV-Vis spectra for the titration of Cu(II) (3.43 mM) with ligand i3A in acetonitrile.
Figure S46. UV-Vis spectra for the titration of Cu(II) (3.43 mM) with ligand i3B in acetonitrile.

Figure S47. UV-Vis spectra for the titration of Cu(II) (3.43 mM) with ligand i3C in acetonitrile.
CD spectroscopic measurements of Cu(II) complexes in acetonitrile (recorded on a Jasco J-815 spectropolarimeter in a 1 cm cuvette) generally showed weak peaks in the visible region (Figures S42-S47), with the exception of i2A and i3A complexes. In general, stronger CD peaks were observed for a ligand:Cu(II) ratio of 1:1, due to the weaker absorbance of ML₂ compared to ML as observed in the UV-Vis titrations. The presence of additional donor groups in the side chain, especially in phenylalanine derivatives B and C, offers many coordination possibilities, making the interpretation of UV and CD results less straightforward.

Figure S48. CD spectra of Cu(II) with different equivalents of b1A, c(Cu²⁺) = 3.22 mM (left) and b2C, c(Cu²⁺) = 3.22 mM (right) in acetonitrile.

Figure S49. CD spectra of Cu(II) with different equivalents of b2A, c(Cu²⁺) = 3.13 mM (left) and b2B, c(Cu²⁺) = 3.13 mM (right) in acetonitrile.
Figure S50. CD spectra of Cu(II) with different equivalents of i2A, c(Cu(II)) = 3.13 mM (left) and i2B, c(Cu(II)) = 3.13 mM (right) in acetonitrile. The peaks of imda complexes could not be completely observed, as the instrument does not give reliable data for wavelengths higher than 750 nm.

Figure S51. CD spectra of Cu(II) with different equivalents of b3A, c(Cu(II)) = 5.56 mM (left) and b3B, c(Cu(II)) = 5.56 mM (right) in acetonitrile.

Figure S52. CD spectra of Cu(II) with different equivalents of i3A, c(Cu(II)) = 5.42 mM (left) and i3B, c(Cu(II)) = 5.42 mM (right) in acetonitrile.
Figure S53. CD spectra of Cu(II) with different equivalents of b3C, c(CuII) = 6.07 mM (left) and i3C, c(CuII) = 6.07 mM (right) in acetonitrile.
8   NMR of Zn(II) complexes

8.1   $^1$H NMR spectra with 0.5 and 1 added equivalents of Zn(CF$_3$SO$_3$)$_2$

Figure S54. $^1$H NMR spectra of b1A (left) and b2C (right) upon addition of Zn(CF$_3$SO$_3$)$_2$ in acetonitrile-$d_3$

Figure S55. $^1$H NMR spectra of b2A (left) and b2B (right) upon addition of Zn(CF$_3$SO$_3$)$_2$ in acetonitrile-$d_3$

Figure S56. $^1$H NMR spectra of i2A (left) and i2B (right) upon addition of Zn(CF$_3$SO$_3$)$_2$ in acetonitrile-$d_3$
Figure SS7. $^1$H NMR spectra of $b3A$ (left) and $b3B$ (right) upon addition of Zn(CF$_3$SO$_3$)$_2$ in acetonitrile-$d_3$

Figure SS8. $^1$H NMR spectra of $i3A$ (left) and $i3B$ (right) upon addition of Zn(CF$_3$SO$_3$)$_2$ in acetonitrile-$d_3$

Figure SS9. $^1$H NMR spectra of $b3C$ (left) and $i3C$ (right) upon addition of Zn(CF$_3$SO$_3$)$_2$ in acetonitrile-$d_3$
8.2 $^{13}$C and 2D NMR spectra of ML complexes

Figure S60. $^{13}$C APT NMR of $[\text{Zn(b2A)}]^{2+}$ (red) and $[\text{Zn(b3A)}]^{2+}$ (blue) in acetonitrile-$d_3$. Carbonyl (’’’), pyridine (*) and chelator methylene carbons (#) are accented.
Figure S61. COSY NMR of [Zn(b3A)]^{2+} (acetonitrile-d₃), aromatic region.

Figure S62. COSY NMR of [Zn(b3A)]^{2+} (acetonitrile-d₃), aliphatic region.
Figure S63. HSQC NMR of [Zn(b3A)]^{2+} (acetonitrile-d₃), aromatic region.

Figure S64. HSQC NMR of [Zn(b3A)]^{2+} (acetonitrile-d₃), aliphatic region.
8.3 ¹H NMR spectra of different L : M ratios at -40°C

Figure S65. ¹H NMR (acetonitrile-d₃) spectra at -40 °C of b3A with different equiv. of Zn(CF₃SO₃)₂. From bottom to top: 0.25, 0.5, 0.75, and 2 equiv Zn(II). When larger amounts of Zn(CF₃SO₃)₂ are added, NH₄⁺ appears as a triplet (J = 53 Hz) around 6.0 ppm.

Figure S66. ¹H NMR (acetonitrile-d₃) spectra at -40 °C of b3A with different equiv. of Zn(CF₃SO₃)₂. From bottom to top: 0.25, 0.5, 0.75, and 2 equiv Zn(II).
Figure S67. COSY NMR of $[\text{Zn(b3A)}_2]^{2+}$ (acetonitrile-$d_3$) at -40 °C (aromatic region). The second diastereomer is denoted (*).
8.4 Variable temperature $^1$H NMR spectra of complexes at a L : Zn(II) ratio of 2 L : 1

Figure S68. VT $^1$H NMR (acetonitrile-d$_3$) of b$_{2C}$ (left) and b$_{2A}$ (right) with 0.5 equiv. Zn(II)

Figure S69. VT $^1$H NMR (acetonitrile-d$_3$) of b$_{3A}$ (left) and b$_{2B}$ (right) with 0.5 equiv. Zn(II)
Figure S70. VT $^1$H NMR (acetonitrile-$d_3$) of $b_3A$ with 0.5 equiv. Zn(II), c(L) = 10.9 mM. Side chain amide NH protons (*) are accented. A small amount of free ligand is observed with a pyridine peak at 8.50 ppm.

Figure S71. VT $^1$H NMR (acetonitrile-$d_3$) of $b_3B$ with 0.5 equiv. Zn(II), c(L) = 11.6 mM. Side chain amide NH protons (*) are accented. A small amount of free ligand is observed with a pyridine peak at 8.47 ppm.
Figure S72. VT $^1$H NMR (acetonitrile-d$_3$) of i3A with 0.5 equiv. Zn(II), c(L) = 14.6 mM. Side chain amide NH protons (*) are accented.

Figure S73. VT $^1$H NMR (acetonitrile-d$_3$) of i3B with 0.5 equiv. Zn(II), c(L) = 5.0 mM. Side chain amide NH protons (*) are accented.
8.5 $^{13}$C APT NMR spectra of complexes at a L : Zn(II) ratio of 2 : 1

Figure S74. $^{13}$C APT (acetonitrile-$d_3$) spectra of L and ML$_2$ for ligand b3A. Pyridyl (*) and chelator methylene (%) carbons are accented.

Figure S75. $^{13}$C APT (acetonitrile-$d_3$) spectra of L and ML$_2$ for ligand b3B. Pyridyl (*) and chelator methylene (%) carbons are accented.
Figure S76. $^{13}$C APT (acetonitrile-$d_3$) spectra of L and ML₂ for ligand i3A. Chelator methylene (#) carbons are accented.

Figure S77. $^{13}$C APT (acetonitrile-$d_3$) spectra of L and ML₂ for ligand i3B. Chelator methylene (#) carbons are accented.
For these NMR measurements, ML complexes with zinc(II) triflate were prepared in acetonitrile, evaporated to dryness, then dissolved in 30 µL of deuterated DMSO and diluted with 600 µL of D$_2$O.

Figure S78. NOESY NMR of ML complex [Zn(b2A)]$^{2+}$ (D$_2$O) (aromatic region). Chemical exchange peaks are denoted green.
Figure S79. NOESY NMR of ML complex [Zn(b3A)]^{2+} (D_{2}O) (aromatic region).
Figure S80. UV-Vis titration of b2A (57.1 µM) with CuCl2 in a 20:1 water : DMSO mixture.

Figure S81. Curve fitting and species distribution for the titration of b2A (57.1 µM) with CuCl2 in a 20:1 water : DMSO mixture. The species distribution is shown for 5 mM concentration of CuCl2 as was used in the DNA cleavage experiments.
Figure S82. UV-Vis titration of b3A (28.6 µM) with CuCl₂ in a 20:1 water : DMSO mixture.

Figure S83. Curve fitting and species distribution for the titration of b3A (28.6 µM) with CuCl₂ in a 20:1 water : DMSO mixture. The species distribution is shown for 5 mM concentration of CuCl₂ as was used in the DNA cleavage experiments.
10 Computational analysis

Figure S84. Evolution of distances between selected ligand atoms and Zn(II) cation in the matching ML complexes in the acetonitrile solution during MD simulations. In both cases, Cl\(^-\) anions are used as counterions, which both coordinate Zn(II) cations during simulations.
Figure S85. Structures of the most stable ML₂ isomers involving Zn(II) cations and selected ligands as obtained by the (SMD)/M05–2X/6–31+G(d)/LanL2DZ+ECP model.
Figure S86. Optimized structure of the cis-fac [Zn(b3B')2]2+ complex with the indicated hydrogen bonding contact among the side chain amide groups as obtained by the (SMD)/M05-2X/6-31+G(d)/LanL2DZ+ECP model. During MD simulations, these hydrogen bonding interactions are recorded in 18% of the simulation structures.
11 DNA cleavage

Acetonitrile and $N,N$-dimethylformamide were tested as weakly coordinating solvents\textsuperscript{7,8} for preparation of stock solutions, but retention of the reaction mixture in the gel was observed in these experiments. Therefore, DMSO was used for the preparation of stock solutions.

Figure S87. (A) Agarose gel (0.5% in TAE buffer) electrophoresis patterns of pUC19 DNA (20 ng/µL) incubated with designated complexes dissolved in acetonitrile in 2.5 (first lane) and 5 mM (second lane) concentrations. C1 represents the native pUC19 plasmid incubated in reaction buffer; NC represents the reaction buffer alone. (B) Agarose gel (0.5% in TAE buffer) electrophoresis patterns of pUC19 DNA (20 ng/µL) incubated with designated complexes dissolved in $N,N$-dimethylformamide (DMF) at 2.5 and 5 mM concentrations. C represents the native pUC19 plasmid incubated in reaction buffer; NC represents the reaction buffer alone; all samples were incubated for 1 h at 37 °C.
Figure S88. Agarose gel (0.5% in TAE buffer) showing cleavage of pUC19 DNA (20 ng/μL) incubated with 2.5 (first lane) and 5 mM (second lane) complexes [CuCl₂(b2A)] - [CuCl₂(i3C)] in 25 mM Tris buffer/50 mM NaCl, pH 7.4. DNA ladder with a distinct high intensity band of 3 kb is followed by reactions of pUC19 with the complexes, followed by control reactions; +PstI reaction represents the native pUC19 plasmid linearized by PstI endonuclease; C1 represents the native pUC19 plasmid incubated with reaction buffer and complex solvent (DMSO); C2 represents the native pUC19 plasmid incubated with reaction buffer and [CuCl₂]; all samples were incubated for 1 h at 37°C.

In reactions with the tested complexes, most prominent examples being plasmid DNA incubations with [CuCl₂(i3A)] and [CuCl₂(i3C)], the intensity of the supercoiled DNA bands was diminished without a significant increase in the linear DNA portion, with visible smears of DNA (Figure S83). Such smears have been observed in literature and are attributed to unwinded and partially unwinded plasmid conformations due to DNA charge neutralization, covalent DNA cross-linking, or both effects combined, resulting in conformational changes, as well as to the possibility of degradation of all DNA forms to smaller fragments.⁸⁻¹⁰
Figure S89. Agarose gel (0.5% in TAE buffer) electrophoresis patterns of pUC19 DNA (20 ng/µL) incubated with 2.5 mM and 5 mM of selected bpa and imda ligands in 25 mM Tris buffer/50 mM NaCl, pH 7.4. C1 - native pUC19 plasmid in reaction buffer, C2 – blank reaction buffer; all samples were incubated for 1 h at 37°C.

Figure S90. Agarose gel (0.5% in TAE buffer) electrophoresis patterns of pUC19 DNA (20 ng/µL) incubated with 2.5 mM and 5 mM of selected metal complexes in 25 mM Tris buffer/50 mM NaCl, pH 7.4. C1 - native pUC19 plasmid in reaction buffer, C2 – blank reaction buffer; all samples were incubated for 1 h at 37°C. Retention of the reaction mixture in the gel was observed for [ZnCl₂(i2A)] and [Cu(i3A)₂]Cl₂, possibly due to precipitation of the complex in the reaction buffer.
Figure S91. (A) Agarose gel (0.5% in TAE buffer) electrophoresis patterns of pUC19 DNA (20 ng/µL) incubated with 2.5 and 5 mM complexes [CuCl₂(i2B)] and [CuCl₂(b2C)], followed by electrophoresis patterns of the same reactions with the addition of different radical scavengers (KI, NaN₃ and tBuOH) in equimolar ratios to the complexes (1:1). +PstI reaction represents the native pUC19 plasmid linearized by PstI endonuclease. C represents the native pUC19 plasmid incubated in reaction buffer. The lower gel shows electrophoresis patterns of pUC19 DNA (20 ng/µL) incubated with radical scavengers (KI, NaN₃ and tBuOH) alone. (B) Electrophoresis patterns of pUC19 DNA (20 ng/µL) incubated with 2.5 and 5 mM complexes [CuCl₂(i2B)] and [CuCl₂(b2C)], followed by electrophoresis patterns of the same reactions with the addition of excess DMSO (1:100 and 1:2000), followed by control reactions with just pUC19 and excess DMSO (1:100 and 1:2000 for both conditions). +PstI reaction represents the native pUC19 plasmid linearized by PstI endonuclease; C represents the native pUC19 plasmid incubated in reaction buffer. All samples were incubated in 25 mM Tris buffer/50 mM NaCl, pH 7.4, for 1 h at 37 °C.
Figure S92. The results of pUC19 DNA cleavage catalyzed by [Cu(i2B)Cl$_2$] (A) and [Cu(b2C)Cl$_2$] (B) with the addition of different radical scavengers (KI, NaN$_3$, tBuOH) in equimolar ratios (1:1). The results of pUC19 DNA cleavage catalysed by [Cu(i2B)Cl$_2$] (C) and [Cu(b2C)Cl$_2$] (D) with the addition of excess DMSO (1:100 and 1:2000). (E) Control reactions of pUC19 DNA incubated with radical scavengers (KI, NaN$_3$, tBuOH, DMSO) alone. +PstI represents the native pUC19 plasmid linearized by PstI endonuclease; C represents the native pUC19 plasmid incubated in the reaction buffer. All samples were incubated in 25 mM Tris buffer/50 mM NaCl, pH 7.4 for 1 h at 37 °C. The representative electrophoresis gels are shown in Figure S84.
12 Characterization of the precursors and ligands

12.1 $^1$H NMR spectra of precursors Boc2A-Boc3C:

![$^1$H NMR spectra of Boc2A](image1)

Figure S93. $^1$H NMR (300.13 MHz, CDCl$_3$) of Boc2A

![$^1$H NMR spectra of Boc2B](image2)

Figure S94. $^1$H NMR (300.13 MHz, CDCl$_3$) of Boc2B
Figure S95. $^1$H NMR (600.13 MHz, CDCl$_3$) of Boc3A

Figure S96. $^1$H NMR (600.13 MHz, CDCl$_3$) of Boc3B
Figure S97. $^1$H NMR (300.13 MHz, CDCl$_3$) of Boc3C
12.2 $^1$H and $^{13}$C NMR spectra of ligands b1A-i3C:

Figure S98. $^1$H NMR (300.13 MHz, CD$_3$CN) of b1A

Figure S99. $^{13}$C NMR (75.47 MHz, CD$_3$CN) of b1A
Figure S100. $^1$H NMR (300.13 MHz, CD$_3$CN) of b2C

Figure S101. $^{13}$C NMR (75.47 MHz, CD$_3$CN) of b2C
Figure S102. $^1$H NMR (300.13 MHz, CD$_3$CN) of b2A

Figure S103. APT $^{13}$C NMR (150.90 MHz, CD$_3$CN) of b2A
Figure S104. $^1$H NMR (300.13 MHz, CD$_3$CN) of b2B

Figure S105. APT $^{13}$C NMR (150.90 MHz, CD$_3$CN) of b2B
Figure S106. $^1$H NMR (600.13 MHz, CD$_3$CN) of i2A

Figure S107. APT $^{13}$C NMR (150.90 MHz, CD$_3$CN) of i2A
Figure S108. $^1$H NMR (300.13 MHz, CD$_3$CN) of i2B

Figure S109. APT $^{13}$C NMR (150.90 MHz, CD$_3$CN) of i2B
Figure S110. $^1$H NMR (600.13 MHz, CD$_3$CN) of b3A

Figure S111. APT $^{13}$C NMR (150.90 MHz, CD$_3$CN) of b3A
Figure S112. ^1^H NMR (600.13 MHz, CD$_3$CN) of b3B

Figure S113. APT ^13^C NMR (150.90 MHz, CD$_3$CN) of b3B
Figure S114. $^1$H NMR (600.13 MHz, CD$_3$CN) of i3A

Figure S115. APT $^{13}$C NMR (150.90 MHz, CD$_3$CN) of i3A
Figure S116. $^1$H NMR (600.13 MHz, CD$_3$CN) of 3B

Figure S117. APT $^{13}$C NMR (150.90 MHz, CD$_3$CN) of 3B
Figure S118. $^1$H NMR (600.13 MHz, CD$_3$CN) of b3C

Figure S119. APT $^{13}$C NMR (150.90 MHz, CD$_3$CN) of b3C
Figure S120. $^1$H NMR (300.13 MHz, CD$_3$CN) of 13C

Figure S121. $^1$H NMR (300.13 MHz, CDCl$_3$) of 13C
Figure S122. APT \textsuperscript{13}C NMR (600.13 MHz, CDCl\textsubscript{3}) of i3C
12.3 ESI-MS spectra of ligands

Figure S123. ESI-MS of b1A

Figure S124. ESI-MS of b2C

Figure S125. ESI-MS of b2A

Figure S126. ESI-MS of b2B

Figure S127. ESI-MS of i2A
Figure S128. ESI-MS of i2B

Figure S129. ESI-MS of b3A

Figure S130. ESI-MS of b3B

Figure S131. ESI-MS of i3A
Figure S132. ESI-MS of i3B

Figure S133. ESI-MS of b3C

Figure S134. ESI-MS of i3C

Figure S135. IR (KBr) spectrum of b2A-Cu

13 References


